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<110> Co, Man Sung
        Vasquez, Maximiliano
        Carreno, Beatriz
        Celniker, Abbie Cheryl
        Collins, Mary
        Goldman, Samuel
        Gray, Gary S.
        Knight, Andrea
        O'Hara, Denise
        Rup, Bonita
        Veldman, Geertruida M.
<120> HUMANIZED IMMUNOGLOBULIN REACTIVE WITH B7-2 MOLECULES AND METHODS OF
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Val His Ser gin Val Gin Leu Gin gin Ser Gly Pro Glu Leu Val Arg
                                                                                                        96
cct ggg gaa tca gtg aag att tcc tgc aag ggt tcc ggc tac aca ttc
Pro Gly Glu Ser val Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe
                                                                                                       144
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Thr Asp Tyr Ala Ile Gln Trp val Lys Gln Ser His Ala Lys Ser Leu
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Thr Ala Tyr Met Glu Leu Ala Arg Leu Thr Ser Glu Asp Ser Ala Ile
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Page 1

384

405

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Artificial Sequence

wys00401 Sequence_Listing.txt

WYS00401_Sequence_Listing.txt
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gtg tca gca gga gag aag gtc act atg agc tgc aaa tcc agt cag agt val Ser Ala Gly Glu Lys val Thr Met Ser Cys Lys Ser Ser Gln Ser
ctg ctc aac agt aga acc cga gag aac tac ttg gct tgg tac cag cag Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln 50
aaa cca ggg cag tct cct aaa ctg ctg atc tac tgg gca tcc act agg $$$ Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg 65 $$$ 70 $$$ 80 $$$
gaa tct ggg gtc cct gat cgc ttc aca ggc agt gga tct ggg aca gat 288 Glu Ser Gly Var Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp
ttc act ctc acc atc agc agt gtg cag gct gaa gac ctg gca gtt tat Phe Thr Leu Thr I'le Ser Ser Val Gin Ala Glu Asp Leu Ala Val Tyr 100 100 110
tac tgc acg caa tct tat aat ctt tac acg ttc gga ggg ggg acc aag Tyr Cys Thr Gin Ser Tyr Asn Leu Tyr Thr Phe Gly Gly Thr Lys 115 120 120
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wys00401 Sequence Listing.tx

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Leu Leu Asn 50	Ser Arg Thr	Arg Glu Asn 55	Tyr Leu Ala 60	Trp Tyr	Gln Gln
Lys Pro Gly 65	Gln Ser Pro 70	Lys Leu Leu	Ile Tyr Trp 75	Ala Ser	Thr Arg 80
Glu Ser Gly	Val Pro Asp 85	Arg Phe Thr	Gly Ser Gly 90	Ser Gly	Thr Asp 95
Phe Thr Leu	Thr Ile Ser 100	Ser Val Gln 105	Ala Glu Asp	Leu Ala 110	Val Tyr
Tyr Cys Thr 115	Gln Ser Tyr	Asn Leu Tyr 120	Thr Phe Gly	Gly Gly 125	Thr Lys
Leu Glu Ile 130	Lys				
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gtg cac tcc Val His Ser	cag gtc cag Gln Val Gln 20	ctg gtg cag Leu Val Gln 25	tct ggg gct Ser Gly Ala	gag gtg Glu Val 30	aag aag 96 Lys Lys
cct ggg agc Pro Gly Ser 35	tca gtg aag Ser Val Lys	gtg tcc tgc Val Ser Cys 40	aaa gct tcc Lys Ala Ser	ggc tac Gly Tyr 45	aca ttc 144 Thr Phe
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gag tgg att Glu Trp Ile 65	gga gtt att Gly Val Ile 70	aat att tac Asn Ile Tyr	tat gat aat Tyr Asp Asn 75	aca aac Thr Asn	tac aac 240 Tyr Asn 80
cag aag ttt Gln Lys Phe	aag ggc aag Lys Gly Lys 85	gcc aca atg Ala Thr Met	act gta gac Thr Val Asp 90	aag tcg Lys Ser	acg agc 288 Thr Ser 95
aca gcc tat Thr Ala Tyr	atg gaa ctt Met Glu Leu 100	agt tct ttg Ser Ser Leu 105	aga tct gag Arg Ser Glu Page 4	gat acg Asp Thr 110	gcc gtt 336 Ala Val

384 405

tat tac tgt gca aga gcg gcc tgg tat atg gac tac tgg ggt caa ggt Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gln Gly 115 120 125
acc ctt gtc acc gtc tcc tca Thr Leu val Thr Val Ser Ser 130 135
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val His Ser Gln val Gln Leu val Gln Ser Gly Ala Glu val Lys Lys 25 30
Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe $\begin{array}{cccccccccccccccccccccccccccccccccccc$
Thr asp Tyr Ala Ile Gln Trp val Arg Gln Ala Pro Gly Gln Gly Leu 50
Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn $65 \ \ 70 \ \ 80$
Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Thr Ser $90 \\$
Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val $100 \\ 0.05$
Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gln Gly 115 125
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wys00401_Sequence_Listing.txt

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gta agc tta Val Ser Leu 35	gga gag agg Gly Glu Arg	gcc act att Ala Thr Ile 40	agc tgc aaa tcc Ser Cys Lys Ser 45	agt cag agt Ser Gln Ser	144
ctg ctc aac Leu Leu Asn 50	agt aga acc Ser Arg Thr	cga gag aac Arg Glu Asn 55	tac ttg gct tgg Tyr Leu Ala Trp 60	tac cag cag Tyr Gln Gln	192
aaa cca ggg Lys Pro Gly 65	cag cct cct Gln Pro Pro 70	aaa ctg ctg Lys Leu Leu	atc tac tgg gca Ile Tyr Trp Ala 75	tcc act agg Ser Thr Arg 80	240
gaa tct ggg Glu Ser Gly	gtc cct gat Val Pro Asp 85	cgc ttc agt Arg Phe Ser	ggc agt gga tct Gly Ser Gly Ser 90	ggg aca gat Gly Thr Asp 95	288
ttc act ctc Phe Thr Leu	acc atc agc Thr Ile Ser 100	agt ctg cag Ser Leu Gln 105	gct gaa gac gtg Ala Glu Asp Val	gca gtt tat Ala Val Tyr 110	336
tac tgc acg Tyr Cys Thr 115	Gln Ser Tyr	aat ctt tac Asn Leu Tyr 120	acg ttc gga cag Thr Phe Gly Gln 125	i Giy inr Lys	384
gtg gaa ata Val Glu Ile 130					396

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Artificial Sequence

Humanized murine anti-human B7-2 light chain

<400> 8

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Val Ser Leu Gly Glu Arg Ala Thr Ile Ser Cys Lys Ser Ser Gln Ser 40

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wys00401_sequence_Listing.txt
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Lys Pro Gly Gln Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg 65 \hspace{1.5cm} 70 \hspace{1.5cm} 75 \hspace{1.5cm} 80
Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr
            100
Tyr Cys Thr Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gln Gly Thr Lys
val Glu Ile Lys
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<212>
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       CDR1 of humanized murine anti-human B7-2 heavy chain
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       10
Asp Tyr Ala Ile Gln
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        11
        51
<211>
<212>
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                                                                                     51
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Gly
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Gly
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(1)..(21)
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Ala Ala Trp Tyr Met Asp Tyr
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<211>
<212> PRT
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<400> 14

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wys00401_Sequence_Listing.txt
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      15
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1 10 15
                                                                                 48
                                                                                 51
gct
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<211>
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      CDR1 of humanized murine anti-human B7-2 light chain
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Ala
<210> 17
<211>
       21
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Trp Ala Ser Thr Arg Glu Ser
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<210> 18
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       CDR2 of humanized murine anti-human B7-2 light chain
<223>
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<211>
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<211>
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<400> 20
Thr Gln Ser Tyr Asn Leu Tyr Thr
<210> 21
<211> 405
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<223> Anti-B7-2 heavy chain
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Met Gly Trp Asn Cys Ile Ile Phe Phe Leu val Thr Thr Ala Thr Gly
                                                                                       48
gtg cac tcc cag gtc cag ctg cag cag tct ggg cct gag ctg gtg agg
Val His Ser Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Arg
                                                                                       96
cct ggg gaa tca gtg aag att tcc tgc aag ggt tcc ggc tac aca ttc
Pro Gly Glu Ser Val Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe
                                                                                       144
act gat tat gct ata cag tgg gtg aag cag agt cat gca aag agt cta
                                                                                       192
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wys00401_sequence_Listing.txt Thr Asp Tyr Ala Ile Gln Trp Val Lys Gln Ser His Ala Lys Ser Leu 50 60 gag tgg att gga gtt att aat att tac tat gat aat aca aac tac aac Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn 65 70 80 240 cag aag ttt aag ggc aag gcc aca atg act gta gac aaa tcc tcc agc Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Ser Ser Ser 90 95 288 aca gcc tat atg gaa ctt gcc aga ttg aca tct gag gat tct gcc atc Thr Ala Tyr Met Glu Leu Ala Arg Leu Thr Ser Glu Asp Ser Ala Ile 100 100 10336 tat tac tgt gca aga gcg gcc tgg tat atg gac tac tgg ggt caa gga Tyr Tyr Cys Ala Arg Ala Ala Trp Tyr Met Asp Tyr Trp Gly Gln Gly 125 384 acc tca gtc acc gtc tcc tca Thr Ser Val Thr Val Ser Ser 130 135 405 <210> 22 <211> 135 <212> PRT <213> Artificial Sequence

<223> Anti-B7-2 heavy chain <400> 22

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WYS00401_Sequence_Listing.txt
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ggt acc tgt ggg gac att gtg ctg tca cag tct cca tcc tcc ctg gct
Gly Thr Cys Gly Asp Ile Val Leu Ser Gln Ser Pro Ser Ser Leu Ala
20 25 30
                                                                                                    96
gtg tca gca gga gag aag gtc act atg agc tgc aaa tcc agt cag agt
val Ser Ala Gly Glu Lys val Thr Met Ser Cys Lys Ser Ser Gln Ser
                                                                                                    144
ctg ctc aac agt aga acc cga gag aac tac ttg gct tgg tac cag cag Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln 50
                                                                                                    192
aaa cca ggg cag tct cct aaa ctg ctg atc tac tgg gca tcc act agg Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg 65 ^{75}
                                                                                                    240
gaa tct ggg gtc cct gat cgc ttc aca ggc agt gga tct ggg aca gat Glu Ser Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp 90 95
                                                                                                    288
ttc act ctc acc atc agc agt gtg cag gct gaa gac ctg gca gtt tat
Phe Thr Leu Thr Ile Ser Ser val Gln Ala Glu Asp Leu Ala Val Tyr
                                                                                                    336
tac tgc acg caa tct tat aat ctt tac acg ttc gga ggg ggg acc aag Tyr Cys Thr Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gly Gly Thr Lys 115 120
                                                                                                    384
                                                                                                    396
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Leu Glu Ile Lys
      130
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<400> 24
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Val Ser Ala Gly Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser
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Leu Leu Asn Ser Arg Thr Arg Glu Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg 66 Fro Gly Val Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp 90 Phe Thr Leu Thr Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Thr Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys $\frac{1}{130}$

<210> 25 <211> 405

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<220> <223> Humanized murine anti-human B7-2 heavy chain

<220> <221> CDS <222> (1)..(405)

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gtg cac tcc cag gtc cag ctg gtg cag tct ggg gct gag gtg aag aag 96 Val His Ser Gin Val Gin Leu Val Gin Ser Giy Ala Giu Val Lys Lys 20 25 30

cct ggg agc tca gtg aag gtg tcc tgc aaa gct tcc ggc tac aca ttc Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe 45

act gat tat gct ata cag tgg gtg aga cag gct cct gga cag ggc ctc $\,$ 192 Thr Asp Tyr Ala Ile Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu $\,$ 50 $\,$ 60

gag tgg att gga gtt att aat att tac tat gat aat aca aac tac aac 240 Glu Trp Ile Gly Val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn 65 75 80

cag aag ttt aag ggc aag gcc aca atg act gta gac aag tcg acg agc $\,$ 288 Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Thr Ser $\,$ 90 $\,$ 95

aca gcc tat atg gaa ctt agt tct ttg aga tct gag gat acg gcc gtt 336 Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val 100 105 110

tat tac tgt gca aga gcg gcc tgg tat atg gac tac tgg ggt caa ggt 384 Page 13

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405

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10
11
15
Val His Ser Gln val Gln Leu val Gln Ser Gly Ala Glu val Lys Lys
Pro Gly Ser Ser val Lys val Ser Cys Lys Ala Ser Gly Tyr Thr Phe
45
Thr Asp Tyr Ala Ile Gln Trp val Arg Gln Ala Pro Gly Gln Gly Leu
55
Glu Trp Ile Gly val Ile Asn Ile Tyr Tyr Asp Asn Thr Asn Tyr Asn
65
Gln Lys Phe Lys Gly Lys Ala Thr Met Thr Val Asp Lys Ser Thr Ser
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ggc acc tgt ggg gac att gtg ctg aca cag tct cca gat tcc ctg gct 96 Page 14

Gly	Thr	Cys	Gly 20	Asp	īle	٧a٦	wys0 Leu	0401 Thr 25	_Seq Gln	uenc Ser	e_Li Pro	stin Asp	g.tx Ser 30	t Leu	Ala	
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aaa Lys 65	cca Pro	ggg Gly	cag Gln	cct Pro	cct Pro 70	aaa Lys	ctg Leu	ctg Leu	atc Ile	tac Tyr 75	tgg Trp	gca Ala	tcc Ser	act Thr	agg Arg 80	240
gaa Glu	tct Ser	ggg G1y	gtc val	cct Pro 85	gat Asp	cgc Arg	ttc Phe	agt Ser	ggc Gly 90	agt Ser	gga Gly	tct Ser	ggg Gly	aca Thr 95	gat Asp	288
ttc Phe	act Thr	ctc Leu	acc Thr 100	atc Ile	agc Ser	agt Ser	ctg Leu	cag Gln 105	gct Ala	gaa Glu	gac Asp	gtg val	gca Ala 110	gtt val	tat Tyr	336
tac Tyr	tgc Cys	acg Thr 115	caa Gln	tct Ser	tat Tyr	aat Asn	ctt Leu 120	tac Tyr	acg Thr	ttc Phe	gga Gly	cag Gln 125	999 G1y	acc Thr	aag Lys	384
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wys00401_Sequence_Listing.txt
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Ala val Tyr Tyr Cys ser Gln Ser Tyr Asn Leu Tyr Thr Phe Gly Gln

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120

Page 19

386

438

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wys00401_sequence_Listing.txt

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wys00401_sequence_Listing.txt

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194

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wys00401_sequence_Listing.txt

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Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys 290 300 Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Val Val Ser Val Leu 305 310 315Thr Val Val His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys 325 330 335 Val Ser Asn Lys Gly Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys $340 \hspace{1.5cm} 345 \hspace{1.5cm} 350$ Thr Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser \$355\$Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys 370 375 380Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln 385 390395 Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Met Leu Asp Ser Asp Gly 405Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln 420 $$ 425Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn 445 His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 450 455 460

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Dago 20	

actctgtgaa gggccgattc accatctcca gaggcaacgc caagaactca ctgtatctgc aaatgaacag cctgagagcc gaggacacgg ccgtgtatta ctgtgcgaga gggatctgtc ttatgacaga ggctactttg actactgggg ccagggaacc ctggtcaccg tctcctca 240 300 358

<210> 51 <211> 97 <212> PRT

<213> Artificial Sequence

<220> <223> III2R variable Heavy Chain

<400> 51

Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser Ser 10 15

Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met Gly 35 40 45

Arg Ile Met Pro Ile Leu Gly Leu Ala Asn Tyr Ala Gln Lys Phe Gln $_{50}^{\rm CO}$

Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr Met 65 70

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala $85 \hspace{0.5cm} 90 \hspace{0.5cm} 95$

Arg

<210> 52 <211> 98

<212> PRT <213> Artificial Sequence

<220> <223> H2F Variable Heavy Chain

<400> 52

val Gln Leu val Glu Ser Gly Gly Gly Leu val Lys Pro Gly Gly Ser $1 \ \ \, 10 \ \ \, 15$

Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr Tyr $20 \hspace{1cm} 25 \hspace{1cm} 30$

Met Ser Trp Ile Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ser 35 40 45

Tyr Ile Ser Ser Arg Gly Ser Glu Thr Ile Tyr Tyr Ala Asp Ser Val $50 \ \ \,$

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys $85 \hspace{1cm} 90 \hspace{1cm} 95$

Ala Arg